

## **Derivation of an RfC for Libby Amphibole**

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**Region 8**

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**DRAFT DO NOT CITE OR QUOTE**

## **Epidemiological Studies in Scott's Marysville Facility**

- Libby Amphibole was used in the facility from 1957 until 1980
- Original study published in 1984 (Lockey et al., Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite, Am Rev Respir Dis 129:952-958)
- University of Cincinnati Research Time conducted a follow-up study of those workers still living in 2004
- UC Team made the unpublished data available to Region 8 in 2006

## **Exposure Reconstruction**

- **Industrial hygiene data from 11 areas in the Marysville facility**
- **Fibers analyzed by polarized light microscopy with dispersion staining**
- **Fibers also analyzed by scanning electron microscopy with energy dispersive x-ray analysis and transmission electron microscopy with selected area electron diffraction**
- **Particles with a length greater than 5 microns, a diameter less than 3 microns, and an aspect ratio of 3:1 or greater were counted as fibers**
- **Obtained exposure history for each worker from an interview to determine time spend in each work area**

## **Exposure Reconstruction**

- **Fiber concentration in work areas ranged from 0.049 to 1.511 fibers/cc**
- **Duration of exposure ranged from 9 weeks to more than 23 years**
- **The study was conducted in 2004, more than 20 years after the facility stopped using Libby Amphibole**
- **The calculated exposure ranged from 0.00778 to 28.1 fibers-year/cc**

## Health Outcome

- Interview to determine health history
- Spirometry
- Pulmonary examination
- Chest x-ray analyzed using ILO (2000) criteria for discrete pleural thickening, diffuse pleural thickening, and parenchymal changes

## UC Data by Quartile

All Workers

Quartile	Fiber-year/cc	N	Discrete Pleural Thickening only	Diffuse Pleural Thickening	Parenchymal Change
1 <sup>st</sup>	0.00778 - 0.28	70	5	0	0
2 <sup>nd</sup>	0.29 - 0.95	70	14	0	0
3 <sup>rd</sup>	0.96 - 2.42	70	22	1	1
4 <sup>th</sup>	2.42 - 28.10	70	23	11	7
Total		280	64	12	8

## UC Data by Quartile

Workers with No Previous Exposure to Asbestos

Quartile	Fiber-year/cc	N	Discrete Pleural Thickening only	Diffuse Pleural Thickening	Parenchymal Change
1 <sup>st</sup>	0.00778 - 0.28	63	4	0	0
2 <sup>nd</sup>	0.29 - 0.95	63	10	0	0
3 <sup>rd</sup>	0.96 - 2.42	63	22	1	1
4 <sup>th</sup>	2.42 - 28.10	63	20	9	6
Total		252	56	10	7

## UC Data by Quartile

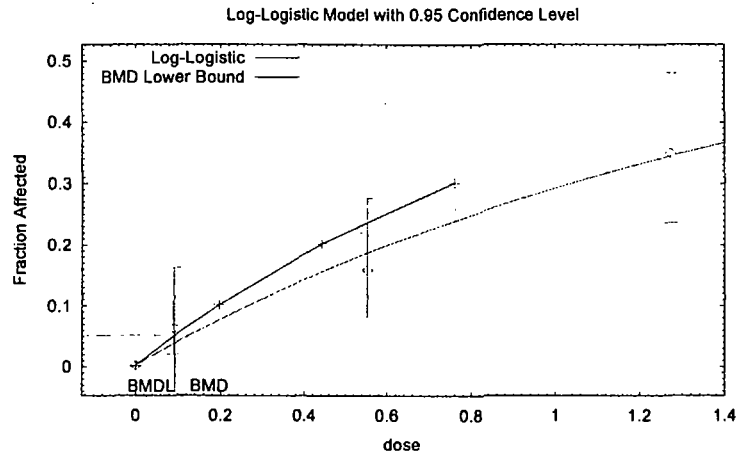
Workers with No Previous Exposure to Asbestos

Statistical Analysis

Quartile	Fiber-year/cc	N	Discrete Pleural Thickening only	Crude Odds Ratio	95% CI
1 <sup>st</sup>	0.00778 - 0.28	63	4	Reference	—
2 <sup>nd</sup>	0.29 - 0.95	63	10	2.78	0.82, 9.40
3 <sup>rd</sup>	0.96 - 2.42	63	22	7.92	2.54, 24.68
4 <sup>th</sup>	2.42 - 28.10	63	20	6.86	2.19, 21.52
Total		252	56		

## BMC Analysis

excluding top exposure and with added background  
(3/1422)



$BMC_{05} = 0.1279$   
 $BMCL_{05} = 0.0931$

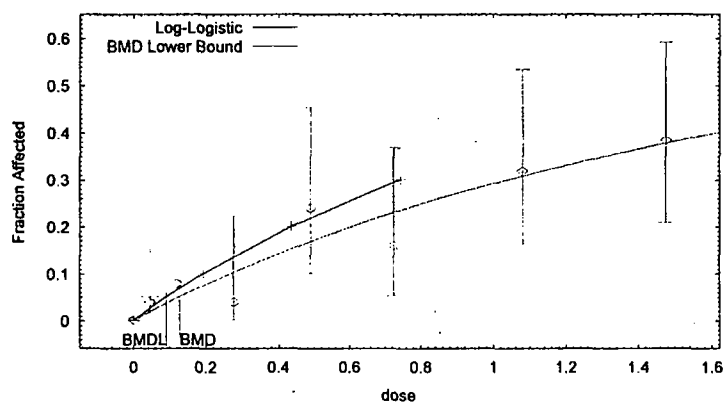
## Region 8 Groupings

Median Fibers-year/cc	Discrete Pleural Thickening	Diffuse Pleural Thickening	Parenchymal Change	Any Radiographic Change
0.0452	1/25	0/25	0/25	1/25
0.1210	2/25	0/25	0/25	2/25
0.2762	1/25	0/25	0/25	1/25
0.4894	6/25	0/25	0/25	6/25
0.7246	4/25	0/25	0/25	4/25
1.0807	8/25	0/25	0/25	8/25
1.4749	10/26	0/26	0/26	10/26
2.4137	9/25	1/25	2/25	9/25
4.3012	11/25	4/25	0/25	11/25
16.5226	17/26	5/26	5/26	18/26

## BMC Analysis

Region 8 groupings, excluding top 3 exposures and  
with added background (3/1422), slope  $\geq 1$

Log-Logistic Model with 0.95 Confidence Level



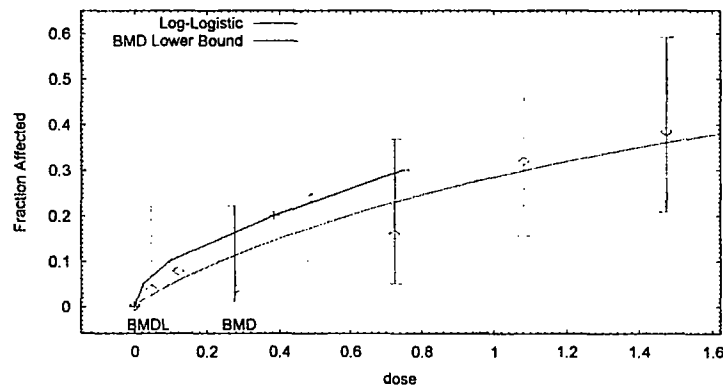
11:46 01/08 2007

$BMC_{05} = 0.1280$   
 $BMCL_{05} = 0.0916$

## BMC Analysis

Region 8 groupings, excluding top 3 exposures and  
with added background (3/1422), slope not restricted

Log-Logistic Model with 0.95 Confidence Level



12:35 01/08 2007

$BMC_{05} = 0.1037$   
 $BMCL_{05} = 0.0232$

## **Calculation of the Human Equivalent Concentration**

The UC exposure reconstruction is for an 8 hour TWA exposure and needs to be adjusted to continuous exposure (24 hours/day, 365 days/year)

EPA's usual practice is to adjust an occupational study using a correction factor of

$$10 \text{ m}^3/20\text{m}^3 \times 5 \text{ days}/7 \text{ days or } 0.357$$

## **Calculation of the Human Equivalent Concentration**

- UC Research Group assumed each individual worked each calendar day in the year.
- The workers did not work a normal 40 hour work week.
- Detailed work records are not available.

## **Calculation of the Human Equivalent Concentration**

**Region 8 assumed a reasonable range of work shifts to be:**

- 1) 6 months at 10 hrs/day, 6 days/wk, and 6 months at 8 hrs/day, 5 days wk**
- 2) 4 months at 12 hrs/day, 6 days/wk, and 8 months at 8 hrs/day, 5 days/wk**
- 3) 12 months at 8 hrs/day, 7 days/wk**
- 4) 12 months at 8 hrs/day, 6 days/wk**
- 5) 12 months at 8 hrs/day, 5 days/wk**

## **Calculation of the Human Equivalent Concentration**

- Region 8 made the judgment that scenarios 1, 2, and 4 were the most probable and scenarios 3 and 5 were the least probable.**
- Region 8 used the geometric mean adjustment factor from these three scenarios to derive the correction factor of 0.442344.**

## **Uncertainty Factors**

- **Interspecies:** Not used, based on human study
- **Intraspecies:** 10, no data available to depart from the default value
- **LOAEL/NOAEL:** Not used, based on BMD analysis
- **Data base:** 1, but no studies for other potential critical effects

## **Calculation of the RfC for Cumulative Exposure**

$$\text{RfC} = 0.0915651 \times 0.442344 \times 1/10$$

$$\text{RfC} = 0.004 \text{ fibers-year/cc}$$

**Where 0.0915651 = POD**

**0.442344 = adjustment to  
continuous exposure**

**10 = Uncertainty factor for human  
variability**

**The RfC for cumulative exposure of 0.004 fibers-year/cc can be used for any scenario (acute to chronic) that includes duration and concentration dependent exposure to Libby Amphibole.**

**It should not be used for acute and short term exposure if additional future exposure is anticipated.**

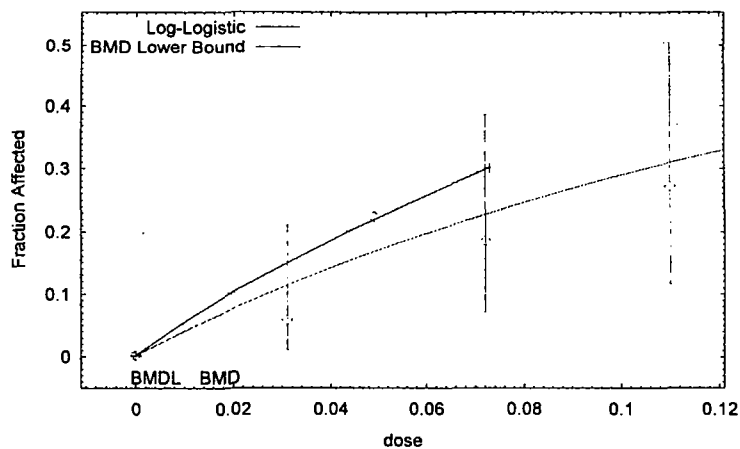
**For some assessments it is useful to have an RfC expressed in concentration units only.**

**As the UC Group provided the duration of exposure for each worker, this calculation is possible.**

## Data Used

Median Fibers/cc	Discrete Pleural Thickening	Diffuse Pleural Thickening	Discrete or Diffuse Pleural Thickening
0.031	2/34	0/34	2/34
0.049	15/67	0/67	15/67
0.072	5/27	0/27	5/27
0.11	5/22	1/22	6/22

## Log-Logistic Model with 0.95 Confidence Level



13:05 01/08 2007

$$\mathbf{BMC}_{05} = 0.0130$$
$$\text{BMCL}_{05} = 0.0092$$

## **Calculation of the RfC as Fibers/cc**

$$\text{RfC} = 0.00924967 \times 0.442344 \times 1/10$$

$$\text{RfC} = 0.0004 \text{ fibers/cc}$$

**Where 0.0924967 = POD**

**0.442344 = adjustment to continuous  
exposure**

**10 = Uncertainty factor for human  
variability**

**The RfC of 0.0004 fibers/cc  
applies to subchronic and  
chronic exposure**

## **Next Steps**

- **Revise document in response to internal reviewer comments**
- **External Peer Review Workshop**
- **Incorporate into IRIS Assessment**